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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/820,530	04/07/2004	Dennis Benjamin	PPI-144	8326

959 7590 10/13/2006

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EXAMINER	
PERREIRA, MELISSA JEAN	

ART UNIT	PAPER NUMBER
1618	

DATE MAILED: 10/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/820,530	BENJAMIN ET AL.	
	Examiner	Art Unit	
	Melissa Perreira	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 August 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/10/04,9/6/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Specification

1. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: The structure of the instant claim 18 is omitted from the specification whereas the chain of the compound of the instant claim 18 is different than the compound of formula II (spec., p12).

Claim Objections

2. Claim 17 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Instant claim 16 recites a fumagillin analogue comprising a biotin moiety where as the dependent claim 17 recites a structure that does not provide a biotin moiety.

3. Claim 19 is objected to because of the following informalities: The indication of the steps of claim 19 are (a) and (2) and should either be altered to read (a) and (b) or (1) and (2). Appropriate correction is required.

4. Claims 17 and 18 are objected to because of the following informalities: The instant claims 17 and 18 fail to end in a period as is required. Appropriate correction is required.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-3,9,10,19,20 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear as to which test compound or biological target to use for the method of measuring the ability of a test compound to inactivate a biological target in the instant claims 1-3,9,10,19,20 and 22. The administration of different compound will vary with regards to dose or the biological target of interest.

3. Claims 15-18 recite the limitation " the quantifiable irreversible MetAP-2 inhibitor". There is insufficient antecedent basis for this limitation in the claim. The instant claim 1 to which they depend does not mention a quantifiable irreversible MetAP-2 inhibitor.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 19-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Turk (*Chem. Biol.* **1999**, *6*, 823-833).

6. Turk et al. (*Chem. Biol.* **1999**, *6*, 823-833) teaches of the treatment of bovine aortic endothelial cells with fumagillin analog, TNP-470 that are then lysed for determination of unbound MetAP2. These lysates were treated with biotin-fumagillin, labeling MetAP2 protein that remained unbound following TNP-470 treatment. Bound biotin was detected by probing the membrane with streptravidin-horseradish peroxidase, and the signal was competed by cell treatment with increasing concentrations of TNP-470 (p824, results). The inhibition of MetAP2 was examined in several human cell lines, such as HeLa, Jurkat T lymphocytes and HT1081C (p825, paragraph 1).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-17 and 19-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Turk et al. (*Chem. Biol.* **1999**, *6*, 823-833) and Amitai et al. (WO02/065977).

9. Turk et al. (*Chem. Biol.* **1999**, *6*, 823-833) teaches of the treatment of bovine aortic endothelial cells with fumagillin analog, TNP-470 that are then lysed for determination of unbound MetAP2. These lysates were treated with biotin-fumagillin, labeling MetAP2 protein that remained unbound following TNP-470 treatment. Bound

biotin was detected by probing the membrane with streptravidin-horseradish peroxidase, and the signal was competed by cell treatment with increasing concentrations of TNP-470 (p824, results). The inhibition of MetAP2 was examined in several human cell lines, such as HeLa, Jurkat T lymphocytes and HT1081C (p825, paragraph 1). Turk et al. (*Chem. Biol.* **1999**, *6*, 823-833) does not teach of the administration of the fumagillin analog to a subject or removing a biological sample from the subject.

10. Amitai et al. (WO02/065977) discloses the treatment of recombinant human acetylcholineesterase, fetal bovine serum-AchE or purified human plasma butyrylcholinesterase with test compounds and their activity measured. The in vivo inhibition of whole blood Che in mice was measured by injecting the tested compounds to the animals then sampling the blood via eye orbit vein (p76).

11. At the time of the invention it would have been obvious to one ordinarily skilled in the art to use the method of measuring the inhibition of MetAP2, such as disclosed by Turk et al. (*Chem. Biol.* **1999**, *6*, 823-833) by administering the fumagillin analog to mice then collecting the whole blood, as disclosed by Amitai et al. (WO02/065977) since mice have a genetic similarity to humans and are frequently utilized for in vivo testing and in vivo testing is the next logical application after studying the properties of a compound in vitro.

12. Claims 1-17 and 19-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Griffiths et al. (*Proc. Natl. Acad. Sci.* **1998**, *95*, 15183-15188) and Morain et al. (*Br. J. Clin. Pharmacol.* **2000**, *50*, 350-359).

13. Griffiths et al. (*Proc. Natl. Acad. Sci.* **1998**, *95*, 15183-15188) discloses the incubation of recombinant human MetAP2 with ovalicin followed by incubation with fluorescein-fumagillin analog. The samples were dialyzed, alkylated, digested and subjected to HPLC separation. The absorbance of each eluate was monitored and the fractions corresponding to peaks for the binding of the fluorescein-fumagillin analog to the MetAP2 were collected (p15184, identification of the covalently modified MetAP2 residue by using fluorescein-fumagillin). It is disclosed that fumagillin and ovalicin covalently bind and inhibit MetPA2 (abstract). Griffiths et al. (*Proc. Natl. Acad. Sci.* **1998**, *95*, 15183-15188) does not disclose the administration of ovalicin, a fumagillin analog to a subject or removal of a biological sample from a subject.

14. Morain et al. (*Br. J. Clin. Pharmacol.* **2000**, *50*, 350-359) discloses the assessment of pharmacodynamics for an inhibitor of prolyl endopeptidase (S 17092) (p350, method). The inhibitor was administered to patients and several parameters were measured, including the activity of prolyl endopeptidase in plasma. The collection of venous blood was measured for S 17092 concentrations and assessment of plasma PEP activity (p351, protocol; p352, sample collection). Controls were used and it was concluded that (S 17092) had a potent, dose-dependent inhibitory effect (p350, conclusion).

15. At the time of the invention it would have been obvious to one ordinarily skilled in the art to utilize the method to identify the binding/inhibition of MetAP2 to/by a quantifiable irreversible inhibitor, such as fluorescein-fumagillin, Griffiths et al. (*Proc. Natl. Acad. Sci.* **1998**, *95*, 15183-15188) where as Morain et al. (*Br. J. Clin. Pharmacol.* **2000**, *50*, 350-359) discloses the administration of an inhibitor to patients and collecting blood to measure the inhibition. It is quite obvious to further test a compound's properties in vivo after assessing their properties, such as binding or inhibition in vitro.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melissa Perreira whose telephone number is 571-272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MP
September 12, 2006

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER